Lack of Quadriceps Dysfunction in Women with Early Knee Osteoarthritis

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Received 2 July 2009; accepted 25 September 2009
Published online 13 November 2009 in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/jor.21038

ABSTRACT: Quadriceps dysfunction, specifically weakness and central activation failure (CAF), has been implicated in the development and progression of knee osteoarthritis (OA), though few data are available to confirm its presence in early OA. The purpose of this study was to determine the presence and magnitude of quadriceps dysfunction in those with and without early knee OA. Thirty-five female volunteers were classified into two groups, OA (n = 22) and control (n = 13), based on the presence [Kellgren-Lawrence (K-L) grade 2] or absence (K-L grade 0–1) of mild OA, respectively. Isometric quadriceps strength and central activation ratio (CAR) were assessed and compared between groups utilizing a one-way ANOVA. Frequency statistics and Fisher’s exact test were used to compare the percentage of women with and without CAF between groups. Quadriceps strength (control: 1.47 ± 0.62 Nm/kg; OA: 1.30 ± 0.62 Nm/kg; p = 0.45) was not significantly different for women with and without mild OA. Further, the CAR (control: 0.91 ± 0.07; OA: 0.87 ± 0.12; p = 0.19) did not differ between groups; however, women in both groups presented with CAF (control: 54%; OA: 73%; p = 0.29). Our results suggest that the women with mild osteoarthritis do not present with quadriceps dysfunction. © 2009 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 28:595–599, 2010

Keywords: osteoarthritis; activation failure; knee

Tibiofemoral osteoarthritis (OA) is a common, debilitating disease. It is estimated that approximately 12% of adults aged 60 and older in the United States have symptomatic knee OA, while over 37% of individuals in that age group present with radiographic evidence of the disease.1 OA is a multifactorial pathology, with a variety of possible contributing factors, including genetic,2,3 metabolic,4 and biomechanical5,6 components. Among these purported contributors to disease initiation and progression is quadriceps dysfunction [i.e., weakness and central activation failure (CAF)].

Quadriceps weakness is a common clinical sign of knee OA7,8 that may contribute to its development and progression. During weight bearing, the quadriceps contract eccentrically to absorb energy.9 When the quadriceps are weakened, their ability to absorb energy is diminished and increased loads are borne by other structures within the knee joint (e.g., the articular cartilage), which may initiate the disease process or enable its progression.10

One possible contributor to quadriceps weakness is CAF. CAF decreases the ability to completely activate a muscle by prohibiting recruitment of all motor units or by failing to achieve maximal discharge rate from the motor units that have been recruited.11 As the knee joint provides sensory feedback to the central nervous system, it is surmised that joint damage alters this sensory information, leading to transmission of an inhibitory signal to the quadriceps α-motoneuron pool, ultimately decreasing voluntary muscle activity.12 In the case of knee OA, joint pain,13 effusion,14 and damage to joint structures associated with the disease14,15 may initiate quadriceps CAF. Previous research has demonstrated the presence of CAF in individuals with symptomatic as well as moderate-to-severe radiographic knee OA,9,16,17 suggesting that CAF contributes to quadriceps weakness in the later stages of the disease process. CAF has, in fact, been demonstrated to more strongly predict quadriceps weakness than lean muscle cross-sectional area in individuals with severe OA.18 If CAF does contribute to the quadriceps weakness present in individuals with knee OA, it seems that CAF could be involved in the degenerative process, though few data are available to support its role in the early stages of the disease. Therefore, the purpose of this study was to determine the presence and magnitude of quadriceps dysfunction in women with and without mild tibiofemoral OA. We hypothesized that women with mild OA would demonstrate greater quadriceps weakness and CAF than women without OA.

METHODS
Participants
Volunteers were identified while participating in an ongoing clinical trial to improve quadriceps strength in women with knee OA. From the total of 46 available women, 35 were enrolled in this study. Based on literature examining activation failure in persons with and without OA, we determined that at least seven participants per group were necessary to achieve 80% statistical power with an α-level of 0.05 and an effect size of 1.46.19 Two groups, mild OA (n = 22) and control (n = 13), were identified based on their medial tibiofemoral compartment Kellgren-Lawrence (K-L) score from bilateral radiographs. Women with K-L scores of 0–1 (absence or doubtful presence of radiographic OA) were classified as not having knee OA and were assigned as controls. Those women with K-L grade 2 (mild radiographic features of OA) were classified as having early knee OA. The limb with the higher K-L score was taken as the test limb. In
participants with equal K-L scores bilaterally, the more symptomatic limb was chosen as the test limb. Subjective symptoms were assessed using the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC), wherein participants rated their symptoms on a scale from 1–5 (none to extreme). Participants were excluded if they were morbidly obese [body mass index (BMI) ≥ 40 kg/m²] or had moderate-to-severe OA (K-L grades 3–4). Demographic information can be found in Table 1. This study was approved by the University of Michigan Health Sciences Institutional Review Board. All participants provided written, informed consent prior to participation.

Radiographic Assessment
Participants completed bilateral, weight-bearing, plain radiograph assessment in a semi-flexed position (Model X-GE MPX-80; General Electric, Milwaukee, WI). Radiographs were read for knee OA characteristics and classified according to the K-L scale by one of the investigators (MFS) and a musculoskeletal radiologist. If agreement on the K-L score was not reached between the two readers, radiographs were re-read and, if required, subjected to consensus reading by another musculoskeletal radiologist. Inter-reader reliability was high (kappa = 0.92). Precise details of the x-ray procedures and K-L assessment methods are described elsewhere.

Quadriceps Strength and Central Activation

Failure Assessment
Participants were seated on an isokinetic dynamometer (Biodex System 3, Biodex Medical Systems, Shirley, NY) with the hip flexed to 85° and the knee flexed to 90°. Each woman was secured to the dynamometer with the test leg being fixed to the dynamometer arm and straps securing the thigh and pelvis. Three repetitions of a knee extension maximal voluntary isometric contraction (MVIC) were performed with 2-min rest provided between repetitions to limit the effects of fatigue on the measurement. The torque signal was exported and, if required, subjected to consensus reading by another musculoskeletal radiologist. Inter-reader reliability was high (kappa = 0.92). Precise details of the x-ray procedures and K-L assessment methods are described elsewhere.

Statistical Analysis
Separate 1 × 2 analyses of variance (ANOVA) were performed to compare group means for each of the dependent variables (quadriceps strength and CAR), as well as compare demographics information between the two groups. A frequency table was generated to identify the number of women in each group with none–mild and moderate–severe scores on the WOMAC pain subscale, as well as the number of women with and without CAF in each group. Fisher’s exact test was used to determine if the frequencies for pain and CAF differed for each group. The α-level was set a priori at p ≤ 0.05 for all tests.

RESULTS
Participant demographics were similar between groups (Table 1). Peak quadriceps strength did not differ between groups [control: 1.47 ± 0.62 Nm/kg, median = 1.34 Nm/kg, 95% confidence interval (CI) = 1.11–1.82; mild OA: 1.30 ± 0.62 Nm/kg, median = 1.22, 95% CI = 1.03–1.57; p = 0.45] (Fig. 1). Further, no statisti-
central activation ratio for each group.

Figure 2. Average (+SE) peak quadriceps central activation ratio for each group.

cally significant group mean differences were identified for quadriceps CAR (control: 0.91 ± 0.07, median = 0.93, 95% CI = 0.86–0.97; mild OA: 0.87 ± 0.12, median = 0.90, 95% CI = 0.82–0.91; p = 0.19) (Fig. 2). CAF was present in 54% of control and 73% of OA participants (p = 0.29) (Table 2). Knee pain was either absent or mild in severity in 77% of control and 64% of OA participants for the WOMAC pain subscale (p = 0.48) (Table 2).

DISCUSSION

Quadriceps dysfunction is often implicated in the initiation and progression of knee OA; yet evidence of its presence early in the disease process is lacking. Our study is the first to examine if quadriceps activation failure is present in women with mild/early osteoarthritis. Establishing the presence of quadriceps dysfunction, or lack thereof, in women with early evidence of the disease may lend to a better understanding of whether it is indeed plausible that quadriceps dysfunction appears in the initial stages of the disease process and could contribute to its onset and progression. Our findings suggest that quadriceps dysfunction is not different between healthy women and those with early OA, calling into question the previously presented hypothesis that quadriceps dysfunction appears in the initial stages of the disease process, as has been suggested.24,27

Contrary to our hypothesis, there was no statistically significant difference in quadriceps strength between the OA and control groups. This finding is in disagreement with previous research demonstrating that individuals without knee OA have greater quadriceps strength than those with OA.7,9,28 Though there is a discrepancy between our results and those of others, the magnitude of the normalized strength values is similar to those reported previously for individuals with and without OA using similar procedures to those of ours.

In disagreement with our hypothesis, our results demonstrated that the magnitude of CAF was not statistically different between women with and without early OA. Previous research examining the relationship between quadriceps CAF and knee OA is conflicting. Several studies have found that individuals with OA demonstrate significantly greater CAF than those without OA, though these studies included individuals with moderate and severe OA (K-L grades 3–4). Our results do agree, however, with those of Lewek et al.9 who found no difference in the CAF between individuals awaiting high tibial osteotomy and healthy controls. While there is some disagreement between our results and those reported previously with regards to CAF, it is worth noting that the magnitudes of CAF previously reported for both healthy and osteoarthritic individuals vary greatly. In fact, higher9,31 and lower16 CAF values compared to the present results have been reported for individuals with OA. Further, the CAR values of our control participants are both similar to32 and lower than9, those reported previously in healthy individuals. Differences in study sample size, participant age, OA severity and symptoms at the time of testing, as well as methodological differences in voluntary activation assessment, not only potentially explain discrepancies between our work and that of other researchers, but also make comparing the results of this study with previous work difficult.

One possible explanation for the lack of difference between groups in both quadriceps strength and CAF is the classification system employed. Participants in our study were grouped according to the traditionally accepted standards regarding the presence or absence of OA, with K-L grades 0–1 representing the absence of OA, though all of our control participants presented with K-L grade 1 radiographs. Evidence is available, however, to suggest that a K-L grade of 1 may represent emergent OA rather than the complete absence of OA. Hart and Spector33 demonstrated that over 60% of individuals with K-L grade 1 radiographs progressed to K-L grade 2 or higher over a 10-year follow-up period. Additionally, our research group22 has reported that women with K-L grade 1 radiographs at baseline were 2.2 times more likely to develop K-L grade 2 or higher OA within 3 years compared with K-L grade 0. Considering these studies, the absence of a statistically significant difference in quadriceps strength and CAF may indicate that K-L grades 1 and 2 actually represent a similar population, those with early OA. If quadriceps weakness is a contributor to the onset of the osteoarthritic disease process, as has been suggested,24,27 then decrements in

Table 2. Knee Pain and Central Activation Failure Frequencya

<table>
<thead>
<tr>
<th>Participant Characteristic</th>
<th>Control Group (n = 13)</th>
<th>OA Group (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOMAC pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None–mild (1–2)</td>
<td>10 (77%)</td>
<td>14 (64%)</td>
</tr>
<tr>
<td>Moderate–severe (3–5)</td>
<td>3 (23%)</td>
<td>8 (36%)</td>
</tr>
<tr>
<td>Central activation failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (CAR &gt; 0.95)</td>
<td>6 (46%)</td>
<td>6 (27%)</td>
</tr>
<tr>
<td>Yes (CAR &lt; 0.95)</td>
<td>7 (54%)</td>
<td>16 (73%)</td>
</tr>
</tbody>
</table>

CAR, central activation ratio; OA, osteoarthritis; WOMAC, Western Ontario McMaster Universities Osteoarthritis Index.

aData are number of cases (percentage of group).
quadriceps functioning would likely arise prior to clinical evidence of OA. As such, we could speculate that CAF and quadriceps strength deficits would occur similarly in both our groups if K-L grade 1 is indeed an indicator of future OA. It is important to keep in mind, however, that we could not ascertain the length of time the women in our study presented with their current K-L score. The amount of time in a disease stage may, in fact, affect the presence or magnitude of quadriceps dysfunction, but this is yet to be determined.

The lack of significant differences between groups in our study may also be attributable to the majority of individuals enrolled reporting mild symptoms, indicating no pain or mild pain on the WOMAC pain subscale. Previous research has demonstrated that knee pain and quadriceps strength and activation are likely inversely related, with increased pain corresponding to greater weakness and CAF. If pain is critical to quadriceps dysfunction initiation, it seems that the similar pain levels in our groups may be an indicator of similar quadriceps strength and activation. Further, though there was no mean difference between the two groups, our participants did present with quadriceps dysfunction, calling into question the belief that pain is a necessary risk factor for muscle dysfunction. Instead, it seems that other factors, such as joint damage, may be a more important contributor than pain to quadriceps dysfunction in the early stages of the disease process.

While there was a lack of significant difference for quadriceps CAF between the OA and control groups, it is important to note that approximately 66% of all participants, regardless of disease state, demonstrated quadriceps CAF. The activation failure present in our study sample may reflect the age-related decline in muscle activation that has been reported previously. Alternatively, if a K-L score of 1 is indeed representative of emergent OA as discussed above, the high frequency of activation failure in our sample may be attributable to the OA disease process. Research examining the prevalence of activation failure in healthy adults across the age span and in osteoarthritic patients in various stages of the disease is also needed to better understand the genesis of OA-related CAF.

It should be noted that the frequency of participants in our study presenting with CAF is dependent upon our operational definition of CAF (a CAR < 0.95). Although this definition of CAF has been utilized previously in the literature, it is important to keep in mind that its clinical meaningfulness is unknown. Whether a person with a CAR of 0.95 or higher has less physical dysfunction than a person with a lower CAR value requires future study. Research also needs to be directed at identifying the magnitude of CAF that results in clinical symptoms and/or biomechanical adaptations.

Quadriceps strength, in addition to its importance in lower extremity biomechanics, may be related to functional performance and knee symptoms. Several researchers have reported that increased quadriceps strength leads to improvements in functional perform-

ance and self-reported knee function, as well as a reduction in symptoms. As both of our groups displayed quadriceps CAF, interventions designed to counter the activation deficits in middle-aged adults may lead to enhanced functional ability and reduced pain in this population.

A potential limitation of this study is the small sample size (control: n = 13; OA: n = 22) employed. While an a priori power analysis revealed the need for a minimum of seven participants per group, it is possible that including additional participants could have yielded statistical significance, suggesting greater quadriceps dysfunction in individuals with mild radiographic OA. However, considering the relatively small effect sizes (quadriceps strength: Cohen’s d = 0.27; quadriceps CAF: Cohen’s d = 0.41), we question whether statistically significant differences in quadriceps dysfunction between groups would be clinically meaningful.

While the burst superimposition technique is a frequently utilized sensitive measurement of muscle activation, it is not without limitations. The CAR derived from the burst superimposition testing has been suggested to overestimate activation failure. Further, an assumption of this and other similar techniques is that participants generate a true maximal voluntary contraction, as failure to do so would result in a greater magnitude of CAF and, accordingly, a lower CAR than is actually present. Despite efforts to maximize participant effort through familiarization with the task and robust verbal encouragement/feedback, it is difficult, if not impossible, to ensure our participants put forth a truly maximal effort.

In conclusion, quadriceps strength and CAF were not different among women with early osteoarthritis (K-L 2) and controls (K-L 0–1). Despite a lack of difference between groups, 66% of participants in our sample demonstrated quadriceps CAF. The presence of activation failure in this sample suggests that quadriceps strengthening interventions may be prudent in middle-aged women. Though our results imply that the magnitude of quadriceps dysfunction does not differ between women with early OA and controls, future studies should consider that a K-L score of 1 may represent emergent OA. Further research, ideally in the form of longitudinal studies, is needed to better elucidate the role of quadriceps dysfunction throughout the knee OA process.

ACKNOWLEDGMENTS
This study was supported by The Michigan Arthritis Foundation grant #N007718 (Palmieri-Smith).

REFERENCES